NICOLA Conference Presentations

2014

Date	14th March 2014
Event/location	Vision TRG Conference, Malone Lodge Hotel, Belfast
Title	Development of Ultra-wide field colour fundus photography grading scheme for use in epidemiological studies to evaluate peripheral lesions
Authors	Quinn, Nicola B.[1]; Aslam, Asma[2]; Lengyel, Imre[2]; Peto, Tunde[3]; Hogg, Ruth
Purpose	Develop a grading scheme to classify peripheral retinal lesions suitable for use in a large epidemiological study
Methods	A grading scheme was developed based on a combination of the Moorfield's grid and the Wisconsin age-related maculopathy grading scheme (WARMGS) grid; additionally eight subfields beyond the standard macular area were defined. A systematic review of potential retinal lesions identified seven key lesions. Validation and inter-grader repeatability was undertaken by two independent graders using images from the Reykjavik Eye Study. Optomap colour images of fifty participants (1 image per eye) were selected randomly from the Reykjavik Eye Study. Percentage of lesions located in the various zones was calculated to inform on optimal design of a peripheral retinal grid.
Results	Agreement for identification of peripheral lesions ranged from 60%-100% (Kappa 0.48-1.0). Agreement was highest for presence or absence of individual retinal lesions (97%-100%, Kappa 0.92-1.0). Greatest variability was for presence of drusen in the various zones (60%-99%), Kappa 0.47-0.70).
Conclusion	In developing a grid for grading peripheral lesions, our findings suggest that the area beyond the traditional WARMGS macula grid should include zones to separate the mid periphery from the far periphery and also include subfields that respect the midline. Therefore we have proposed a grid that includes 16 peripheral sub-fields. This grading scheme showed low variability between graders and therefore should prove suitable for use in a large epidemiological study.
Abstract published	No

Date	7th May 2014
Event/location	ARVO Conference, Orlanda, Florida
Title	Refining the ultra-wide field colour fundus photography grading scheme for use in epidemiological studies

Authors	Quinn, Nicola B.[1]; Aslam, Asma[2]; Lengyel, Imre[2]; Peto, Tunde[3]; Hogg, Ruth E.[1]
Purpose	To develop a grading scheme to classify peripheral retinal lesions suitable for use in a large epidemiological study.
Methods	A grading scheme was developed based on a combination of the Moorfield's grid (which is derived from the International Classification for age-related macular degeneration (AMD)) and the Wisconsin age-related maculopathy grading scheme (WARMGS) grid. These macula centred grids were altered in order to capture information from the peripheral retina. Eight subfields beyond the standard macular area were defined using an extension of the WARMGS sections together with vertical and horizontal lines in both the mid and far periphery. A systematic review of potential retinal lesions identified the following lesions for presence/absence evaluations: choroidal neovascular membrane, geographic atrophy, floaters, naevi, retinal tears, white without pressure and haemorrhages. Drusen and RPE changes were evaluated in terms of which retinal zone they were noted in. Validation and inter-grader repeatability was undertaken by two independent graders using images from the Reykjavik Eye Study. Optomap colour images of fifty participants were selected randomly from the Reykjavik Eye Study, providing 100 images to grade. Percentage of lesions located in the various zones was calculated to inform on optimal design of a peripheral retinal grid.
Results	Agreement for identification of peripheral lesions ranged from 60%-100% (Kappa 0.48-1.0). Agreement was highest for presence or absence of individual retinal lesions (97-100%, Kappa 0.92-1.0). Greatest variability was for presence of drusen in the various zones (60%-99%, Kappa 0.47-0.70). Drusen were most frequently located superiorly (68%). RPE changes were also seen most commonly in the superior sections (63%), in the most peripheral zones (81%) and in those subfields closest to the midline (75%).
Conclusion	In developing a grid for grading peripheral lesions, our findings suggest that the area beyond the traditional WARMGS macula grid should include zones to separate the mid periphery from the far periphery and also include subfields that respect the midline. Therefore we have proposed a grid that includes 16 peripheral sub-fields. This grading scheme showed low variability between graders and therefore should prove suitable for use in a large epidemiological study.
Abstract published	Yes
Abstract reference	Investigative Ophthalmology & Visual Science April 2014, Vol.55, 4818.

Date	7th May 2014
Event/location	ARVO Conference, Orlando, Florida

Title	Can Heidelberg MultiColor images be used interchangeably with color fundus photography for grading age-related macular degeneration features?
Authors	Graham, Katie[3]; Larkin, Patrick[2, 3]; Muldrew, Katherine Alyson[2, 3]; Silvestri, Vittorio [1, 3]; Young, Graham[1, 2]; McIntyre, Philip[1]; McAtamney, Helen[1]; Hogg, Ruth
Purpose	To characterize the appearance of age-related macular degeneration features (AMD) on Heidelberg MultiColor images(MCI) and then systematically compare their appearance with color fundus photography (CFP).
Methods	Study design: Observational case series. Participants: 30 patients attending Macular clinics in Belfast and 30 participants from the Northern Ireland Cohort for the Longitudinal study of aging (NICOLA). Images were obtained after dilation using both CFP and cSLO MCI (Heidelberg Engineering, Germany) using standardized protocols. Color fundus photographs were assessed and clinical features of AMD noted (hard drusen, soft drusen, reticular pseudodrusen, geographic atrophy, haemorrhage and fibrosis), the constituent images from the cSLO imaging were assessed in turn (infrared(IR), green reflectance(GR), blue reflectance(BR) and composite MultiColor) and the presence or absence of the features noted on CFP was determined. Features present on MultiColor and absent on CFP were also noted. Test characteristics were determined and a matrix describing the appearance of AMD features on the different images was constructed. Examples of artefact's were also collected.
Results	A total of 99 eyes with gradable images were available for comparison (56 eyes from patients and 43 eyes from NICOLA study participants). Using CFP as the gold standard, sensitivity values for MCI ranged from 100% for fibrosis to 68% for soft drusen. Specificity values were high (95%+) for all features except hard drusen (75%). For all AMD features except haemorrhage there were instances where features were noted on MCI but not on CFP. When features were present on MCI their edges usually appeared more distinct than on CFP.
Conclusion	Although sensitivity and specificity values were high for most AMD features it is unlikely that these technologies could be used interchangeably. Careful interpretation is also required given the different appearance of features on CFP and MCI. Given the improved definition of features on MCI it may prove most useful in situations where measurement of lesion size is important.
Abstract published	No

Date	October 2014, November 2014

Event/location	October: Paul B. Beeson Career Development Awards in Aging Research Program Annual Meeting, San Diego, US, November: Centre of Excellence Away Day, NI
Title	Diet, retinal microvascular health and cognitive decline and dementia risk: the NICOLA and TILDA studies
Authors	Charlotte E Neville[1], Michelle C McKinley[1], Gareth J McKay[1], Frank Kee[1], Ian S Young[1], P Passmore[1], Chris R Cardwell[1], Rose Anne Kenny[2], Jayne V Woodside[1] [1]Centre of Excellence for Public Health, Queen's University Belfast, Northern Ireland, [2]The Irish Longitudinal Study on Ageing, Trinity College Dublin, Ireland.
Purpose	In the developed world, as life expectancy increases and birth rate declines, the proportion of older people is increasing. As the proportion of older people increases, so will chronic disease incidence. The increasing prevalence of cognitive decline and dementia, and the impact on healthcare systems is a major concern. In 2010, it was estimated that there were 35.6 million people with dementia worldwide with figures estimated to approximately double every 20 y. The ability to identify those at high risk of dementia at an early stage using non-invasive methodology will be important (e.g. by retinal microvascular assessment), whilst strategies to reduce age-related morbidity and chronic disease prevalence will encourage healthy ageing, and have financial and societal benefits. Dietary factors, including fruit and vegetable (FV) intake, have been suggested to play a role in promoting healthy ageing and reducing the risk of cognitive decline. Accurate assessment of dietary intake in older populations is therefore vital to determine this potential role of diet in promoting healthy ageing. However, accurate estimation of dietary intake is difficult, with methods commonly employed (e.g. food frequency questionnaires (FFQ), 24-h recalls and food diaries) each being associated with error. Using multiple dietary assessment methods and/or biomarker approaches may provide a more accurate estimate of true dietary intake, but this has not yet been tested in older populations. The current study explores the association between FV intake, retinal microvascular health and cognitive decline and dementia risk in the Northern Ireland Cohort Longitudinal Study of Ageing (NICOLA) (8,500 subjects, >50 y) and The Irish Longitudinal Study on Ageing (TILDA) (8,504 subjects, >50 y) studies. The study has four aims: 1) to validate the dietary assessment methodology used in NICOLA, using nutritional biomarkers, 2) to test other potential dietary assessment methods that may be particularly suited for older populations, 3) to determine the association between FV status and cognitive decline and dementia risk (cross-sectionally in NICOLA, longitudinally in TILDA) and, 4) to explore the use of retinal microvascular health assessment as a marker of cognitive decline and dementia risk in TILDA.

Methods	The study aims will be addressed by firstly conducting a validation of the FFQ, currently being used in NICOLA, against a 4-day food diary and a panel of biomarkers of FV intake, as objective biological indicators. Secondly, we will conduct a comparison of the multiple 24-h recall method, recently reported to be of use in an older population, with a 4-day food diary in a sub-sample of the NICOLA cohort. Thirdly, we will measure a panel of FV intake biomarkers in both NICOLA and TILDA which will allow us to analyse the association between FV intake biomarkers and measures of cognitive function in NICOLA (cross-sectional), and cognitive decline and dementia risk in TILDA (longitudinal) and to analyse the association between FV intake biomarkers and retinal microvascular parameters, as a possible indicator of cognitive decline. Finally, we will examine the association between retinal microvascular parameters and cognitive decline and dementia risk in TILDA.
Conclusions	This research is aimed at health and social policy makers involved in the promotion of healthy ageing. This research will correct the lack of dietary validation studies in older adults to date. It will also unravel the potential role of diet in healthy ageing and will ultimately lead to appropriate, evidence-based, dietary guidelines for older people to promote healthy ageing, in the context of an ageing population worldwide.

2015

Date	April 2015
Event/location	CARDI (Centre for Aging Research and Development in Ireland; currently known as IPH-Ageing Division) International Scientific Meeting and Leadership Event, Dublin
Title	Diet and cognitive decline and dementia risk
Authors	Neville, C.

2016

Date	19th February 2016 and 3rd May 2016
Event/location	Vision TRG Conference, The Wellcome-Wolfson Building, QUB, Belfast (February) and ARVO Conference, Seattle Washington (May)
Title	Do peripheral retinal lesions impact the vitreo interface in the posterior pole?

Authors	Quinn, Nicola B.1**;** Graham, Katie1; Elliot, David1; Hennessy, Riona1; Wright, D.M.2; Muldrew, Alyson1; Chakravarthy, Usha1; Peto, Tunde3; Hogg, Ruth E.1, NICOLA Study Group
Purpose	To determine the association between peripheral retinal lesions and the presence of vitreomacular adhesions
Methods	Ultra-wide field retinal images (Optomap 200 TX) and corresponding Heidelberg Spectral-Domain OCT retinal images were obtained Northern Ireland Cohort of the Longitudinal Study of Aging (NICOLA Study) participants. Images from 511 participants were assessed. The vitreomacular interface (VMI) was graded for the presence or absence of a vitreomacular adhesion (VMA) using a standardised protocol. The Optomap images were graded for the presence of 16 common retinal lesions, (hard and soft drusen, retinal pigment epithelial (RPE) changes, chorioretinal atrophy, bone spicules, haemorrhages, bear tracks, pavingstone degeneration, naevi, white without pressure, retinoschisis, congenital hypertrophy of the RPE (CHRPE), geographic atrophy (GA), choroidal neovascularisation (CNV), retinal hole and ungradeable area) using the Manchester Grid, which covers the image with 400 boxes, each approximately one disc area in size. Chi-squared tests were used to assess the association between presence of lesions in either the peripheral or central retina and status of the vitreous interface.
Results	960 Optomap and 942 OCT gradeable images were available for analysis. Participants ranged in age from 42 to 96 years (mean 64 years. SD 9.2), 47% were male. Prevalence of VMA within participants in this study was 70% with VMA being relatively evenly distributed between men (70%) and women (68%). Participants with RPE irregularities in their peripheral retina were less likely to have VMA present than those without. In the posterior pole those with hard drusen (p=0.05) or any stage of AMD (p=0.06) tended to be more likely to have VMA present than those without.
Conclusion	RPE irregularities in the periphery appears to be protective for VMA in the posterior pole whereas AMD features occurring in the macular area increase the risk of VMA.
Abstract published	No

Date	3rd May 2016
Event/location	ARVO Conference, Seattle, Washington
Title	Multimodal imaging for geographic atrophy; is colour fundus photography still our gold standard?
Authors	Graham, Katie[3]; Larkin, Patrick[2, 3]; Muldrew, Katherine Alyson[2, 3]; Silvestri, Vittorio [1, 3]; Young, Graham[1, 2]; McIntyre, Philip[1]; McAtamney, Helen[1]; Hogg, Ruth E

Purpose	To describe and characterize the appearance of age-related macular degeneration (AMD) geographic atrophy(GA) lesions on Heidelberg MultiColor images(MCI) and then systematically compare their appearance with color fundus photography (CFP).
Methods	Study design: Observational case series. Participants: 30 patients attending Macular clinics in Belfast and 30 participants from the Northern Ireland Cohort for the Longitudinal study of aging (NICOLA). Images were obtained after dilation using both CFP and cSLO MCI (Heidelberg Engineering, Germany) using standardized protocols. Color fundus photographs were assessed first, and the following sequence of lesion identification was followed: presence or absence of an AMD lesion (active or inactive) and presence or absence of GA. GA lesions were further categorized into atrophy type as follows; inside-lesion, peri-lesion, outside-lesion, combination of inside- and peri-lesion, combination of inside- and outside-lesion, combination of peri- and outside-lesion, and combination of inside-, peri-, and outside-lesion atrophy. Each GA lesion subtype was assigned a numerical code and graded as present or absent. The constituent images from the cSLO imaging were assessed in turn (infrared(IR), green reflectance(GR), blue reflectance(BR) and composite MultiColor) and the presence or absence of lesion, GA and GA subtypes as outlined previously. Features present on MultiColor and absent on CFP were also noted. SD-OCT images were assessed where necessary and when available (OCT capture not a necessity under original imaging protocol). Test characteristics were determined and a matrix describing the appearance of AMD features on the different images was constructed. For image sets showing discordance (GA present on MCI and not on CFP, the presence of GA was confirmed using corresponding OCT where available).
Results	A total of 99 eyes with gradable images were available for comparison (56 eyes from patients and 43 eyes from NICOLA study participants). Cross-tabulation of GA type for each imaging modality was computed. Using CFP as the gold standard, sensitivity for MCI for all GA types was high (96%). Highest sensitivity values were found for inside-lesion atrophy (100%), compared to relatively low values for inside-lesion (40%) and outside-lesion atrophy (50%). For the presence or absence of an AMD lesion, sensitivity was high for MCI compared to CFP (80.56). Specificity values were high (91%+) for all GA subtypes and presence or absence of AMD lesion. It was noted that in all GA detected on MCI, borders and identification had superior definition in comparison to CFP.
Conclusion	Sensitivity and specificity values were high for MCI compared to CFP for the detection of AMD lesion, GA and GA subtypes, with the exception of inside- and outside-lesion atrophy. The improved definition of GA borders on MCI means it has high potential to become a key imaging modality in both clinical and research assessment of patients with GA. However, the interpretation of MCI must be considered carefully due to altered colour appearance in comparison to conventional CFP.
Abstract published	No

2017

Date	8th May 2017
Event/location	ARVO Conference, Baltimore, Maryland
Title	Prevalence and characteristics of peripheral retinal lesions in an ageing population.
Authors	Quinn, Nicola B; Wright, D.M; Peto, Tunde; Cruise, S.M; Young, I.S.; Kee, Frank, Chakravarthy, Usha; Hogg, Ruth E.
Purpose	To determine the prevalence and spatial distribution of peripheral retina lesions and their associated risk factors in a population based sample of ageing individuals.
Methods	Ultra-wide field retinal images (Optomap 200 TX) were obtained from the Northern Ireland Cohort of the Longitudinal Study of Aging (NICOLA Study) participants. Images from the first 1468 participants were assessed. The Optomap images were graded for the presence of 16 common retinal lesions, (hard and soft drusen, retinal pigment epithelial (RPE) changes, chorioretinal atrophy, bone spicules, haemorrhages, bear tracks, pavingstone degeneration, naevi, white without pressure, retinoschisis, congenital hypertrophy of the RPE (CHRPE), geographic atrophy (GA), choroidal neovascularisation (CNV), retinal hole and ungradeable area) using the Manchester Grid, which covers the image with 400 boxes, each approximately one disc area in size. Descriptive statistics were used to describe the prevalence and spatial distribution of the retinal lesions. Generalised estimating equations were used to determine risk factors associated with each retinal lesion.
Results	A total of 3044 images were available for analysis. Participants ranged in age from 40 to 96 years (mean 64 years. SD 9.02), with male and females making up 48.4% and 51.6% of the sample respectively. Prevalence rates ranged from 0.1% for CNV and snailtrack degeneration to 99.8% for hard drusen. The prevalence of lesions were WWOP (11.6%), RPE changes (17.8%), haemorrhages (6.9%), chorioretinal atrophy (8.2%), naevi (10.9%) and soft drusen (8.2%). Confounder adjusted analysis revealed that soft drusen, RPE changes, naevi and chorioretinal atrophy were associated with increasing age. Haemorrhages were associated with a history of cardiovascular disease. Hard drusen was predominantly seen superiorly, RPE changes in the far nasal periphery and WWOP in the far temporal periphery.
Conclusion	Peripheral retinal abnormalities are common in the older population with varying prevalence rates. Some peripheral lesions appear to show distinct spatial patterns whereas other occur throughout the retina. The mechanisms underlying the spatial distribution are not well understood and deserve further investigation.

Abstract published	Yes
Abstract Ref	Investigative Opthalmology and Visual Science 58(8), 1

Date	June 2017
Event/location	Nutrition Society (Irish Section) Annual Meeting, QUB, Belfast
Title	Validity of fruit and vegetable intake assessed by a food frequency questionnaire (FFQ) in older adults: the Northern Ireland Cohort for the Longitudinal Study of Aging (NICOLA).
Authors	CE Neville, MC McKinley, F Kee, IS Young, CR Cardwell and JV Woodside
Purpose	Accurately assessing dietary intake in older populations is vital to determine the potential role of diet in healthy ageing. However, accurate estimation of dietary intake is difficult, with commonly employed methods each being associated with error [(1)]. Assessing dietary intake in older populations can also be challenging as individuals may not be involved in their own food preparation, may not be physically able to record intakes, or may have cognitive impairments impacting on their ability to accurately recall intake. It is therefore essential that commonly-used dietary assessment methods are validated in older populations. Based on the uncertainty over the utility of a food frequency questionnaire (FFQ) to determine dietary intake in older people, the objective of this study was to assess the relative validity of assessing fruit and vegetable (FV) intake from a FFQ compared with a food diary (FD).
Methods	A sub-sample of 50 participants (aged >50 years) from the Northern Ireland Cohort for the Longitudinal Study of Aging (NICOLA) completed a FFQ and 4-day FD at two time-points (Month 0 and Month 6). Estimates of FV intake were compared between methods using Spearman's correlation coefficients, examining the percentage of participants classified into the same or adjacent quartile of FV intake, weighted kappa and Bland-Altman plots.
Results	At both time-points, median fruit, vegetable and total FV intake were significantly higher in the FFQ than the FD. Significant positive correlations (all $p<0.05$) were observed between the FFQ and FD estimates of FV intake at both time-points (Month 0, r=0.44, 0.52 and 0.46 for fruit, vegetables, total FV, respectively; Month 6 r=0.49, 0.44 and 0.44, respectively). After individuals were put in fourths (based upon quartiles of total FV portions by FD or FFQ), 79% and 85% of participants were classified into the same or adjacent quartile at Month 0 and Month 6, respectively, while weighted kappa showed fair-moderate agreement between methods for FV intake (weighted kappa=0.33 and 0.44 at Month 0 and Month 6, respectively). Bland-Altman plots revealed a widening in limits of agreements, between the FFQ and FD, with higher FV intakes. Significant positive correlations were observed between total FV intakes reported at Month 0 and those reported at Month 6 (r=0.53, $p<0.001$), with

	correlation coefficients being stronger for fruit intake (r=0.65, p<0.001) compared to vegetable intake (r=0.36, p=0.01).
Conclusion	While over-reporting is evident with the FFQ compared to the FD, the results show good comparability between the methods in being able to rank older adults according to their FV intake. Analysis of FV biomarkers within this sample will provide a more objective assessment of FV intake by each method.
Abstract published	Yes
Abstract reference	Proceedings of the Nutrition Society 2017; 76 (OCE3), E113

Date	July 2017
Event/location	IAGG, San Francisco, US
Title	Validity of fruit and vegetable intake assessed by a food frequency questionnaire in older adults
Authors	CE Neville, MC McKinley, F Kee, IS Young, CR Cardwell, JV Woodside
Purpose	Accurately assessing dietary intake in older populations is vital to determine the potential role of diet in healthy ageing. Based on the uncertainty over the utility of a food frequency questionnaire (FFQ) to determine dietary intake in older people, the objective of this study was to validate fruit and vegetable (FV) intake from a FFQ, using a food diary (FD).
Methods	A sub-sample of 50 participants (aged >50y) from the Northern Ireland Cohort for the Longitudinal Study of Aging completed a FFQ and 4-day FD (reference method) at two time-points (Month 0 and Month 6). Estimates of FV intake were compared between methods using Spearman's correlation coefficients, cross-classification, weighted kappa and Bland-Altman plots.
Results	At both time-points, median fruit, vegetable and total FV intake were higher (all p<0.001) in the FFQ than the FD. Positive correlations (all p<0.05) were observed between the FFQ and FD estimates at both time-points (Mo 0, r=0.44, 0.52 and 0.46 for fruit, vegetables, total FV, respectively; Mo 6 r=0.49, 0.44 and 0.44, respectively) while weighted kappa showed fair-moderate agreement between methods for FV intake. Cross-classification indicated that 79% of participants were classified into the same or adjacent quartile. Bland-Altman plots revealed a widening in limits of agreements, between the FFQ and FD, with higher FV intakes.
Conclusion	While over-reporting is evident with the FFQ compared to the FD, the results show good comparability in ranking older adults according to their FV intake. Analysis of FV biomarkers within this sample will provide a more objective assessment of FV intake.
Abstract published	No

Date	May 7-11, 2017
Event/location	ARVO Annual Meeting, Baltimore, MD

Title	Factors influencing circumpapillary retinal nerve fibre layer thickness (cRNFLT) in Northern Ireland Cohort Longitudinal Study of Ageing (NICOLA) study
Authors	Paul McCann, Ruth E Hogg, Augusto Azuara-Blanco, Ian S Young, Frank Kee
Purpose	cRNFLT is influenced by ocular diseases such as glaucoma. Demographic and ocular factors including myopia may also influence cRNFLT. The influence of ocular biomechanical properties on cRNFLT has not been reported previously in an adult population based study. We report the association between demographic and ocular biomechanical factors and cRNFLT.
Methods	Cross sectional study: The NICOLA study is an ongoing population-based epidemiological study. The ophthalmic assessment includes: SD-OCT cRNFLT scans, colour stereo pairs of the optic disc and Goldmann-correlated intraocular pressure (IOPg), corneal-compensated intraocular pressure (IOPcc), corneal resistance factor (CRF) and corneal hysteresis (CH) measured using Ocular Response Analyser. Vertical cup-disc ratios (VCDRs) for the first 3001 participants were measured by trained graders who were masked to the cRNFLT measurements. Generalised Estimation Equation (GEE) models were used to enable data from both eyes to be included and multivariable confounder adjusted analysis was performed with the influence of age, sex, IOPg, CH and VCDR explored.
Results	Eyes (n=4375) and participants (n=2486) were included in GEE which demonstrated age (β, -0.139, p<0.001), female gender (β, 2.007, p<0.001), IOPg (β, -0.348, p<0.001) VCDR (per 0.1 increase) (β, -1.0817, p<0.001) and CH (β, 0.366, p=0.022) were significantly associated with cRNFLT. CRF was not associated with cRNFLT in univariate analysis (**r**=0.003, p=0.819) but CH was positively correlated with global cRNFLT in the multivariate analysis.
Conclusion	In addition to age, gender, IOP and VCDR we have identified that lower corneal hysteresis is associated with lower cRNFLT when adjusted for other factors.
Abstract published	Yes
Abstract Ref	Investigative Ophthalmology & Visual Science June 2017, Vol.58, 3136

Date	2017
Event/location	European Congress on Personalised Medicine
Title	Genetic biomarkers in the over 40s in Northern Ireland: evidence from the Northern Ireland COhort of Longitudinal study of Ageing (NICOLA)
Authors	Canadas Garre M, Smyth L, Kee F, Young I, McKnight AJ on behalf of the Northern Ireland COhort of Longitudinal Ageing collaborative group

Purpose	The aim of this study is to identify biomarkers associated with CKD, lipid levels and anthropomorphic traits in older adults in Northern Ireland and to describe a genomic profile of this population.
Methods	This is a cross-sectional study using biomolecular and clinical data from 2,807 patients from the first Wave of data collection in NICOLA. Demographic and clinical information was collected with follow-up interviews planned every two years and health assessments every four years. A range of phenotypes was investigated: CKD (estimated glomerular filtration rate (eGFR), creatinine, cystatin C, CKD stage), lipid levels (total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglyceride (TG) levels), anthropomorphic traits (height, body mass index, waist-hip ratio). DNA was extracted from buffy coats. Genotype data (n=551,839 markers) was generated using Illumina's Infinium CoreExome-24 BeadChips for high-throughput screening on an iScan. Quality control (QC) was performed in PLINK and association analysis (logistic or linear regression) in PLINK and R/SPSS.
Results	Phenotype measures were obtained for 2,529 (kidney measures), 2,543 (lipid levels), and 2,488 (anthropomorphic traits) individuals after QC (Table 1). Age and sex were employed as covariates. Several markers in chromosomes 11, 16, and 19 were significantly associated with lipid levels in this population (Table 2). No association with genome-wide significance was identified for kidney disease or anthropomorphic traits.
Conclusion	Some of the markers identified in this study in older individuals confirm previous associations with lipid levels in other populations. Despite multiple loci being identified in association with eGFR and CKD in both European and non-European populations, those were not replicated in this study, likely as a consequence of the relatively small number of individuals investigated in NICOLA with this phenotype.

Date	2017
Event/location	NIA Biomarker Network Meeting
Title	Analysis of Biomarkers in the Northern Ireland Cohort of Longitudinal study of Ageing (NICOLA)
Authors	McKnight AJ on behalf of the NICOLA collaborative group

Purpose	The NICOLA study was formally launched as Northern Ireland's largest ever public health research project in 2014. This collaborative initiative has finished fieldwork for WAVE 1, collating detailed information on 8,500 local residents over the age of 50 years, with follow-up interviews planned every two years and health assessments every four years. There is a particular focus on multi-omic biomarkers in this relatively early-stage, yet rich resource where additional health and social care information is linked by a unique identifier for each citizen.
Methods	NICOLA created a powerful local biorepository including thirty-four biochemistry-based biomarkers linked to genetic-epigenetic-transcriptomic data. DNA was extracted from buffy coats, while RNA was extracted from PAXgene tubes for all individuals. Genotype data (n=551,839 markers) was generated using Illumina's Infinium CoreExome-24 BeadChips for high-throughput screening on an iScan. Initial quality control was performed in GenomeStudio (v2) with association analysis conducted for a range of phenotypes using PLINK and R. SNPs are being imputed to the Haplotype Reference Consortium. Illumina's Infinium MethylationEPIC BeadChips were employed to quantitatively interrogate >850,000 methylation sites across the genome for 2,000 samples. Data was analysed using GenomeStudio (v2011) with the distribution of methylation levels visualised; concordance rates was excellent ($r>0.99$), and standard quality control was employed prior to further data analysis. mEPIC data is comparable with Sequenom's EpiTYPER results with a low false positive rate where $\Delta\beta \geq 0.2$. RNA-seq data was generated using Ion Torrent's S5XL™ system with both the whole transcriptome and AmpliSeq™ transcriptome (~21,000 targets) approaches; the AmpliSeq protocol has minimal hands on time for 10 ng of input RNA. Quantitative RNA-seq data was analysed using Torrent Suite and Partek Genomics Suite software, with expression compared to that from microarray and qPCR platforms. This robust approach for creating a biomarker repository and developing pipelines for analysis is feasible for larger multi-centre studies.

2018

Date	Abstract submitted May 2018; acceptance TBC
Event/location	American Society of Nephrology
Title	Genetic and epigenetic analysis in genes affecting mitochondrial function are associated with chronic kidney disease in an older population
Authors	Ruaidhri Cappa[1], Laura J Smyth[1], Marisa Canadas Garre[1], Cassio P de Campos[2], Ryan Skelly[1], Bernadette McGuiness[1], Sharon Cruise[1], F Kee[1], Catherine Godson[3], Alexander P Maxwell[1], Amy Jayne McKnight[1] on behalf of the Northern Ireland COhort of Longitudinal Ageing collaborative group.

	1. Epidemiology and Public Health Research Group, Centre for Public Health, Queen's University Belfast, Belfast, United Kingdom 2. Utrecht University 3. University College Dublin
Abstract	The Northern Ireland COhort for the Longitudinal study of Ageing (NICOLA) is a ten-year project exploring health and lifestyle information linked to an extensive bioresource in 8,500 people over the age of 50 years. Chronic kidney disease (CKD) affects ~10% of the World's population and is more prevalent in older individuals. Optimal renal function is heavily dependent upon efficient mitochondria, therefore genetic and epigenetic features that lead to mitochondrial dysfunction may influence CKD. The discovery cohort comprised 2,567 individuals with body mass index ranging from 18.5- 40 kg/m^2. Genotyping was performed using Illumina's Infinium CoreExome array (n=551,839 SNPs directly typed), with data imputed to the Haplotype Reference Consortium. Methylation data was generated using Illumina's Infinium MethylationEPIC array (866,554 features with single site resolution). PLINK and Partek Genomics Suite were employed to investigate association with eGFR, albumin, urea, and creatinine. Replication was conducted in a 402 independent individuals. SNPs that demonstrated the most evidence for association include an exonic SNP in the mitochondrial genome *MT-TL2* gene (-rs2853498; A12308G; a key SNP defining mitochondrial Haplogroup U) with increased creatinine levels (P= 0.000153, OR= 1.185). SNPs in nuclear genes that influence mitochondrial function include rs77790196 within *SLC39A1* (P= 4.4E-07, OR= 0.0055) and rs12564199 within *JTB* (P= 6.6E-07, OR= 0.006) associated with decreased eGFR. Analysis of epigenetic data identified eight genes demonstrating differential methylation with $p<10^{-8}$ and Δβ 0.2, including *ZBED3*), *ZNF672*, and *AHCTF1* for participants with early stage CKD compared to individuals with CKD stages 3-5. These analyses have identified novel associations linking CKD with SNPs and CpG sites. This may serve as a future basis for the development of predictive multi-omic biomarkers and/or increased understanding of CKD pathogenesis.

Date	May 2018
Event/location	European Glaucoma Society Congress, Florence
Title	Glaucoma component of the ophthalmic branch of the NICOLA Study and the Glaucoma within NICOLA (GwNICOLA) study: Methods and rationale
Authors	Paul McCann, Ruth Hogg
Purpose	To present the rationale and methods of the Glaucoma component of the Ophthalmic Branch of NICOLA and GwNICOLA The research questions are: 1. What is the prevalence of glaucoma? 2. What are the socio-economic factors associated with glaucoma? 3. What is the diagnostic accuracy of circumpapillary retinal nerve fibre layer (cRNFL) thickness and macular posterior pole

	asymmetry analysis (PPAA) spectral domain optical coherence tomography (SD-OCT) parameters? 4. Are SD-OCT parameters associated with ocular and demographic factors and cognitive impairment? 5. What are the relationships between structural and functional parameters in GwNICOLA?
Methods	NICOLA: An ongoing longitudinal population-based cohort study comprised of three elements; Computer Assisted Personal Interview (CAPI), self-completion questionnaire (SCQ) and health assessment (HA). CAPI recorded self-reported medical history and sociodemographics. SCQ recorded the National Eye Institute Visual Function Questionnaire (NEI-VFQ-9). HA consisted of anthropometric, cardiovascular, cognitive and ophthalmic tests: Best Corrected Visual Acuity (BCVA), Autorefraction, Tonometry and Biomechanics (ORA), Optic Disc Stereophotography and Spectralis SD-OCT (cRNFL and PPAA). GwNICOLA: A cross-sectional study comprised of a glaucoma-related HA: BCVA, Autorefraction, ORA, Humphrey's Matrix 24-2, Goldmann applanation tonometry (GAT), gonioscopy, biometry, Pentacam, Spectralis SD-OCT (cRNFL and PPAA progression), Spectralis Glaucoma Premium Module Edition (Bruch's membrane opening-minimum rim width [BMO-MRW], cRNFL and PPAA scans), Spectralis OCT-angiography and retinal oximetry (Oxymap T1). International Society Geographical and Epidemiological Ophthalmology (ISGEO) criteria will be used to define glaucoma. Inclusion criteria: NICOLA participants with VCDR ≥0.7 or VCDRA ≥0.2 or NRRR ≤0.1 or IOP ≥25mmHg.
Results	8,504 NICOLA participants from randomly sampled addresses undertook CAPI. Optic disc photographs for 3001 participants and SD-OCT scans for 3182 participants were graded. ORA measurements for 5734 eyes of 2906 participants were analysed. 214 NICOLA participants were eligible for GwNICOLA.
Conclusion	These studies will estimate the prevalence of glaucoma, phenotype glaucoma-related parameters and assess the diagnostic accuracy of imaging technologies in a Northern Ireland population-based study.

Date	6th June 2018
Event/location	Faculty of Public Health Summer meeting (Royal College of Physicians, Ireland)
Title	Harmful and hazardous drinking amongst older people: risk and protective factors
Authors	Michael Donnelly, Dermot O'Reilly, Hannah, Sharon Cruise

Date	2016
Event/location	The Association for Research in Vision and Ophthalmology
Title	Do peripheral retinal lesions impact the vitreo interface in the posterior pole?
Authors	Quinn NB, Graham K, Elliott D, Hennessy R, Wright D, Mudlrew A, Chakravarthy U, Peto T, Hogg RE.
Purpose	To determine the association between peripheral retinal lesions and the presence of vitreomacular adhesions at the fovea.
Methods	Ultra-wide field retinal images (Optomap 200 TX) and corresponding Heidelberg Spectral-Domain OCT retinal images were obtained Northern Ireland Cohort of the Longitudinal Study of Aging (NICOLA Study) participants. Images from 511 participants were assessed. The vitreomacular interface (VMI) was graded for the presence or absence of a vitreomacular adhesion (VMA) using a standardised protocol. The Optomap images were graded for the presence of 16 common retinal lesions, (hard and soft drusen, retinal pigment epithelial (RPE) changes, chorioretinal atrophy, bone spicules, haemorrhages, bear tracks, pavingstone degeneration, naevi, white without pressure, retinoschisis, congenital hypertrophy of the RPE (CHRPE), geographic atrophy (GA), choroidal neovascularisation (CNV), retinal hole and ungradeable area) using the Manchester Grid, which covers the image with 400 boxes, each approximately one disc area in size. Cross tabulation was used to assess the association between presence of lesions in either the peripheral or central retina and status of the vitreous interface.
Results	960 Optomap and 942 OCT gradeable images were available for analysis. Participants ranged in age from 42 to 96 years (mean 64 years. SD 9.2), 47% were male. Prevalence of VMA within participants in this study was 70% with VMA being relatively evenly distributed between men (70%) and women (68%). Participants with RPE irregularities in their peripheral retina were less likely to have VMA present than those without. In the posterior pole those with hard drusen (p=0.05) or any stage of AMD (p=0.06) tended to be more likely to have VMA present than those without.
Conclusion	RPE irregularities in the periphery appears to be protective for VMA in the posterior pole whereas AMD features occurring in the macular area increase the risk of VMA.
Abstract published	Yes
Abstract reference	Investigative Ophthalmology & Visual Science September 2016, Vol.57, 4070. doi:https://doi.org/

Date	27-29th September 2018
Event/location	66th Irish Gerontological Society Annual Scientific Meeting
Title	Frailty and Disability in Ireland North and South: Preliminary evidence from TILDA and NICOLA.
Authors	O'Halloran AM, Cruise S, Roe L, Scarlett S, O'Connell MDL, Kee F, Kenny RA

Purpose	Frailty, a prevalent age-related condition, is a target for disability prevention and intervention in older adults. Previous research indicated higher rates of frailty and disability in Northern Ireland (NI) compared with the Republic (ROI) but may have been vulnerable to data harmonization issues and measurement error. Our objective was to contemporaneously measure the prevalence of frailty and disability using harmonized data from older adults in ROI and NI.
Methods	Secondary analyses were performed on population representative data from adults aged ≥55 years from the third wave of The Irish Longitudinal Study on Ageing (TILDA: n = 6,249; 55% female) and the baseline wave of the Northern Ireland Cohort for the Longitudinal Study of Ageing (NICOLA: n = 6,944; 54% female). TILDA and NICOLA data were collected between February 2014 / March 2016. A Frailty Index (FI) was constructed from thirty harmonized self-report items (frailty: FI ≥ 0.25). Disability was assessed by endorsing ≥1 item from the Instrumental Activities and Activities of Daily Living scales in both cohorts. Prevalence estimates (%; 95% CI) were weighed and standardised to the population aged ≥55 years in NI and ROI.
Results	The estimated prevalence of frailty was 1.6-fold higher in NICOLA (31.3%; 30.3–32.4) compared with TILDA (19.6%: 18.5–20.7). The higher prevalence of frailty in NICOLA was characterized by higher levels of physical limitations, multi-morbidity and poorer emotional health. In NICOLA, the prevalence of any I/ADL disability was 2.2- fold higher (25.2% versus 11.4%). Disability was strongly associated with frailty and was higher among the frail group than among participants aged ≥75 years in both cohorts.
Conclusion	This study highlights marked differences in the prevalence of frailty and disability among adults aged ≥55 years living in the community in NI and ROI. Our findings are the most definitive to date given the large representative cohorts under study and are in keeping with previous research

Date	23-26th October 2018
Event/location	47th European Symposium on Clinical Pharmacy, European Society of Clinical Pharmacy, Belfast
Title	Assessment of patient adherence to long term medications within a large pharmacoepidemiological study using the dried blood spot technique
Authors	Feras J Jirjees, Gaoyun Chen, James C McElnay
Purpose	Pharmaco - epidemiological studies support the rational use of drugs. One of the main obstacles in drawing conclusions relating to safety and effectiveness of medication from this type of study is medication non-adherence, which is a major issue in the management of chronic illness. It is well known that up to 50% of medicines prescribed/dispensed in real life are not taken by patients as recommended by prescribers, with a large proportion of these not taken at all by patients with chronic diseases. The aim of the research is to develop and use a novel direct method to assess medication exposure/adherence in a large cohort study being conducted in Northern Ireland.

Methods	Dried blood spot (DBS) samples collected on Guthrie cards from participants as they join a study. Patients (n=815) who were treated with one of the following drugs was selected: metformin, allopurinol, fluoxetine, bisoprolol, amlodipine and methotrexate. The inclusion criteria of participants are patients with chronic diseases who are ≥ 50 years old. DBS based analytical methods have been developed for the six drugs and/or their metabolites. Fixed volume (15 microliter) DBS samples were used throughout for assay development and for patient samples. Simple solvent extraction approaches were used for four medicines, and solid phase extraction methods used for two drugs. In all cases reversed phase HPLC was utilised with either UV (metformin and allopurinol), fluorescence (fluoxetine and bisoprolol), and mass-spectrometry (amlodipine and methotrexate) detection.
Results	Linear calibration curves were obtained over wide concentration ranges for each of the six drugs, including at levels many times lower than expected steady state trough levels and higher than expected steady state peak levels of the drugs of interest after multiple dosing. All assay methods were shown to have good selectivity, specificity, accuracy and precision according to the international guidelines. A significant proportion of participants (15.3%) within the cohort had no medication of interest in their blood samples, clearly indicating that they were not taking any of the medication at the time of sampling. This was a particular issue for patients using fluoxetine and bisoprolol. Only 57.1% of the patients overall had blood levels within the therapeutic range, indicating that there is significant scope for medication optimisation within the cohort overall
Conclusion	The results of the present study illustrate, for the first time, the possibility of using a DBS sampling approach to assess adherence/exposure to medicines within a large cohort study. The DBS approach was found to be a straightforward, objective approach to assess exposure/adherence to six drugs.

Date	8 Nov 2018
Event/location	Joint Public Health Annual Conference
Title	Frailty and Falls in Ireland North and South: Preliminary evidence from TILDA and NICOLA.
Authors	O'Halloran AM, Cruise S, Roe L, Scarlett S, O'Connell MDL, Kee F, Kenny RA
Abstract	Frailty, a prevalent age-related condition, is a target for disability prevention and intervention in older adults. Previous research indicated higher rates of frailty and disability in Northern Ireland (NI) compared with the Republic (ROI) but may have been vulnerable to data harmonization issues and measurement error. Our objective was to contemporaneously measure the prevalence of frailty and disability using harmonized data from older adults in ROI and NI. Secondary analyses were performed on population representative data from adults aged ≥55 years from the third wave of The Irish Longitudinal Study on Ageing (TILDA: n = 6,249; 55% female) and the baseline wave of the Northern Ireland Cohort for the Longitudinal Study of Ageing (NICOLA: n = 6,944; 54% female). TILDA and NICOLA data were

	collected between February 2014 / March 2016. A Frailty Index (FI) was constructed from thirty harmonized self-report items (frailty: FI ≥ 0.25). Disability was assessed by endorsing ≥1 item from the Instrumental Activities and Activities of Daily Living scales in both cohorts. Prevalence estimates (%; 95% CI) were weighed and standardised to the population aged ≥55 years in NI and ROI. The estimated prevalence of frailty was 1.6-fold higher in NICOLA (31.3%; 30.3–32.4) compared with TILDA (19.6%: 18.5–20.7). The higher prevalence of frailty in NICOLA was characterized by higher levels of physical limitations, multi-morbidity and poorer emotional health. In NICOLA, the prevalence of any I/ADL disability was 2.2- fold higher (25.2% versus 11.4%). Disability was strongly associated with frailty and was higher among the frail group than among participants aged ≥75 years in both cohorts. This study highlights marked differences in the prevalence of frailty and disability among adults aged ≥55 years living in the community in NI and ROI. Our findings are the most definitive to date given the large representative cohorts under study and are in keeping with previous research.
Abstract published	No

Date	29th November 2018
Event/location	22nd European Society for Patient Adherence, Compliance, and Persistence (ESPACOMP) conference (http://espacomp.eu/#toc_2), Dublin
Title	Evaluation of adherence to antihypertension medications using dried blood spot approach
Authors	Feras Jirjees, Gaoyun Chen and James C McElnay
Purpose	Adherence to antihypertensive medication is crucial in the control of blood pressure. Indirect assessment approaches have indicated that adherence to antihypertensive medications ranges from 24.3 to 87.6%. The aim of this study was to develop a direct method to assess adherence to the highly prescribed antihypertensive medications amlodipine and bisoprolol, using dried blood spot (DBS) samples and to use the method in a cohort of patients participating in a large cohort study (NICOLA study)
Methods	HPLC assay methods for DBS samples, using mass spectrometry (amlodipine) or fluorescence (bisoprolol) detection, were developed and validated according to ICH guidelines. DBS samples were collected for 503 hypertensive patients who were prescribed amlodipine or bisoprolol in the primary care setting. All participants were ≥ 50 years old. Fixed volume (15 microliter) DBS samples were used throughout for assay development and for patient samples
Results	The DBS technique was shown to be sensitive and specific for the measurement of amlodipine and bisoprolol concentrations. The limits of quantification of amlodipine and bisoprolol were 0.5 and 4.7 ng/ml, respectively, which are lower than the expected trough level of drug concentrations in blood during routine treatment. The results indicated that 33% of participants had blood concentrations outside the expected therapeutic values, indicating non-adherence. Out

	of the 503 patient samples, 72 had no drug present. Most of the participants (93.6%) who were prescribed one of the selected medications were receiving three or more medications for the treatment of chronic illness (mean 6.7 medications). Generally, there was no association between exposure and non-exposure to the selected medications and number of medications used by the participants.
Conclusion	The methods developed for measuring amlodipine and bisoprolol concentrations in DBS samples were reproducible, accurate and cost-effective for evaluation of drug exposure in patients and thus in evaluating adherence. Non-adherence in this study was estimated to be high, however, it is within the value that is reported previously using indirect methods of adherence assessment.

Date	October 2018
Event/location	Integrating Genomics and the Social Sciences, Boulder, Colorado
Title	An investigation into the DNA methylation patterns of risk and time preference in older individuals
Authors	LJ Smyth, SM Cruise, I Young, B McGuinness, J Tang, F Kee, AJ McKnight on behalf of the Northern Ireland Cohort for the Longitudinal Study of Ageing collaborative group
Purpose	Risk-preference namely our attitude to risk and to decision making under uncertainty, and time preference, the choice between receiving a smaller and immediate reward opposed to a larger and future reward, are complex traits that have both environmental and genetic determinants. We aimed to examine how an individual's risk and time preferences associate with their epigenetic profiles, specifically DNA methylation patterns.
Methods	8,452 participants were recruited as part of the Northern Ireland COhort for the Longitudinal study of Ageing (NICOLA). Risk preferences were ascertained by asking participants to make a series of choices between two hypothetical income scenarios. Data was collected for 4,564 individuals. Income A, which will with certainty give you £1,500 per month for the rest of your life. Income B, which will give you a 50-50 chance of £3,000 and a 50-50 chance of £1,000/£1,200/£1,300 per month for the rest of your life. In total, 1,656 individuals for whom we had DNA methylation and risk preference data, were included in the analysis; 52% were females and 48% were males; four groups were created (quartiles on the risk preference scale) ranging from "risk averse" individuals to "risk seeking" individuals. Time preferences were established by asking participants to make choices between a series of hypothetical scenarios. Data was collected for 4,585 individuals. Would you rather have £1,500 now or £1,506/£1,512/£1,518/£1,524/£1,536/£1,548/£1,596 a month from now? Questionnaire and DNA methylation data was gathered for 1,648 individuals; 52% were females and 48% were males. Eight groups were created, ranging from "patient" to "impatient" individuals. Blood-derived DNA was processed consistently within our single genetics centre. Using the Infinium HD Methylation Assay, MethylationEPIC BeadChips from Illumina evaluated the status of >850,000 CpG sites, promoters and CpG islands. Partek Genomics Suite 7.0 was utilised for data analysis, with standard quality control applied.

Results	We compared the distribution of single site DNA methylation levels in the top and bottom quartiles (risk averse vs risk seeking individuals). A total of 393 CpG sites were identified as having significantly different levels of methylation where $p \leq x10^{-05}$, 101 of which were identified in both males and females. Several genes including CALN1, HLA-DPB1, LIMD1, NWD1 and SEPT4 reported multiple significant CpG sites, none of which had previously been linked to risk aversion. Nicotine addiction was established as the pathway with the greatest enrichment score (17.7), where $p=1.9 x10^{-08}$ in males. A subsequent analysis identified that the methylation values of 61 CpG sites displayed evidence of a linear trend across the risk preference scale. We assessed the methylation levels between the "patient" and "impatient" population groups and identified 94 CpG sites significantly associated with the trait, where $p \leq x10^{-05}$. In total, 16 CpG sites identified were reported in both males and females $P \leq x10^{-03}$. These sites are present within genes including COL1A1, PLEKHG5, STK10 and UXS1, none of which have previously been reported in association to time preference. Population / Participants / Males (%) / Females (%) NICOLA total / 8,452 / 3,775 (44.7) / 4,677 (55.3) Risk preference / 4,564 / 2,015 (44.1) / 2,549 (55.9) Risk preference and methylation / 1,656 / 802 (48.4) / 854 (51.6) Time preference / 4,585 / 2,037 (44.4) / 2,548 (55.6) Time preference and methylation / 1,648 / 799 (48.5) / 849 (51.5)
Conclusion	Epigenetic modifications, including DNA methylation, have not to date been linked to risk aversion and impatience, but may represent important biomarkers of accumulated, but complex genetic and environmental determinants of these traits. Several striking results from this study support further analysis of DNA methylation as an important link between measurable biomarkers and health behaviours. Data from longitudinal cohorts provide the opportunity to monitor the relationship between the two, over time.

Date	October 2018
Event/location	American Society of Nephrology / San Diego, California
Title	An investigation into the DNA methylation patterns of chronic kidney disease in older individuals
Authors	LJ Smyth, SM Cruise, J Kilner, AP Maxwell, I Young, B McGuinness, F Kee, AJ McKnight on behalf of the Northern Ireland Cohort for the Longitudinal Study of Ageing collaborative group
Purpose	Changes in DNA methylation are associated with chronic diseases. The study assessed whether methylation status of CpG sites differs between individuals with and without CKD between the ages of 60 and 79

Methods	Participants were recruited as part of the Northern Ireland COhort for the Longitudinal study of Ageing (NICOLA), a large-scale population-based prospective cohort study. Estimated GFR was calculated for each individual (n=1,097) using the CKD-EPI formula. CKD stages, based on eGFR, were determined and all individuals with stage 2 CKD (eGFR >60 - <90mL/min/1.73m^2) were removed to increase discrimination between CKD case and control groups. Using the Infinium HD Methylation Assay, MethylationEPIC BeadChips from Illumina, the methylation status of >850,000 CpG sites, gene bodies, promoters and CpG islands were determined in each individual. Blood-derived DNA was processed consistently within our single genetics centre. Partek Genomics Suite 7.0 was utilised for data analysis, with standard quality control applied. In total, 155 individuals had CKD stages 3, 4 or 5 and were compared with 240 individuals with eGFR >90ml/min/1.73m^2 and no evidence of renal disease.
Results	In total, 306 CpG sites were identified as having significantly different levels of methylation in individuals with CKD compared with controls ($p<1x10^{-07}$). Among the genes identified with altered methylation status, several, including *CLU*, *NOS3*, *IQSEC1* and *NPHP4* have been linked with CKD. High concordance between duplicate samples was also observed for this array. Three of the significantly associated CpG sites demonstrated a graduated increase in the methylation fold change with worsening renal function i.e. comparing control individuals with persons having CKD stages 3, 4 and 5 respectively.
Conclusion	Epigenetic modifications, such as DNA methylation, may represent important biomarkers for the loss of kidney function in individuals with CKD. Data from this longitudinal cohort study provides the opportunity to monitor and assess the relationship between methylation status and CKD over time with a view to identifying new biomarkers or expanding knowledge of those previously identified CKD biomarkers.

2019

Date	February 2019
Event/location	6th General Assembly of the Marie Curie Alumni Association Vienna
Title	Assessing adherence to the Mediterranean Diet: New tools, biomarkers and associations with healthy ageing
Authors	Brian Green
Purpose	Current dietary assessment methods employ food diaries and questionnaires, which although useful under certain circumstances, have long been deemed inaccurate measuring tools for nutritional intake. The current project aims to use a comprehensive metabolomics approach to identify novel nutritional biomarker candidates of Mediterranean diet. The aim is to help confirm existing biomarkers while discovering novel ones, and to investigate their possible associations with healthy aging phenotypes.

Methods	This is being carried out through the analysis of serum, urine and saliva samples obtained from a dietary validation cohort within NICOLA (The Northern Ireland Longitudinal Study of Ageing). A combined NMR and LC-MS-based metabolomics approach is being undertaken, to take full advantage of both methods' complementary features and to generate high-quality data. Nutritional information was collected, together with the samples, at two time-points six months apart. Metabolomic data acquisition is complete and data analysis of the serum samples is now underway.
Results	Initial diet-metabolite correlations are being explored with appropriate exclusions/corrections for potential confounding from factors such as age and gender. Early results indicate several potential biomarkers of dairy and processed meat consumption, but further exploration and validation of the data are required.

Date	22-24th May 2019
Event/location	53rd Annual Scientific Meeting of the European Society for Clinical Investigation
Title	Application of LCMS based metabolomics to identify and validate nutritional biomarkers in a cohort of Northern Irish older adults
Authors	Gonçalo Rosas da Silva, Stewart Graham, Zafer Ugur, Ali Yilmaz, Jayne Woodside, Brian Green
Purpose	Current tools for the assessment of dietary intake, such as food frequency questionnaires and food diaries, can be inaccurate. Metabolomics, an "omics" tool which measures the levels of exogenous and endogenous metabolites, is being increasingly used in nutrition research to elucidate the physiological responses to food consumption.
Methods	Serum samples were collected, alongside food diaries and detailed lifestyle information, from 96 older adults at two separate time points 6 months apart. All subjects were enrolled within NIDAS, a dietary validation cohort within the NICOLA study. Targeted LC-MS metabolomic data were acquired using a Waters TQ-S coupled with an Acquity I-Class UPLC, in conjunction with Biocrates Absolute IDQ p180 metabolomic kits. Data was processed using METIDQ software, and the integrity of the metabolite peaks was verified using MassLynx v4.1. Data distribution, correlation analysis (Spearman's rho), and k-means clustering were performed using SPSS Statistics 25. Multivariate statistical plots (PCA and PLS-DA) and receiver operating characteristic (ROC) curves were produced using MetaboAnalyst 4.0.
Results	A total of 72 food-metabolite correlations were initially found to be statistically significant. After eliminating potential confounding, including age and sex, a total of 9 significant correlations remained. The strongest correlations were found between the consumption of dairy products and specific glycerophospholipids, namely LysoPC aa C20:3 and C16:1. An established biomarker for dairy intake, PC aa C28:1 was validated, but only in male subjects.
Conclusion	LysoPC aa C20:3 and LysoPC aa C16:1 are potential candidates for blood-based biomarkers of dairy consumption, warranting further validation. These metabolites should prove to be valuable auxiliary tools for measuring consumption of dairy products in nutrition studies.

Date	March 2019
Event/location	NICRN Vision Conference, Belfast,
Title	Spectral domain optical coherence tomography (SD-OCT) for the detection of glaucoma in GwNICOLA
Authors	Paul McCann, R Hogg et al
Purpose	To evaluate the diagnostic accuracy of circumpapillary retinal nerve fibre layer (cRNFL) thickness, macular thickness parameters (posterior pole asymmetry analysis (PPAA) and Early Treatment Diabetic Retinopathy Study (ETDRS) grids) and Bruch's membrane opening minimum rim width (BMO-MRW) SD-OCT parameters to detect glaucoma in a sub-population suspected of having glaucoma.
Methods	Participants aged ≥50 years were recruited from the Northern Ireland Cohort for the Longitudinal Study of Ageing (NICOLA) to the Glaucoma within NICOLA study (GwNICOLA). NICOLA participants with a vertical cup to disc ratio (VCDR) ≥0.7 and/or VCDR asymmetry ≥0.2 and/or neuroretinal rim ≤0.1 and/or IOP ≥25 mmHg were eligible. Glaucoma was defined according to clinical exam by an expert and visual field testing. Index tests included cRNFL, cRNFL Anatomical Positioning System, BMO-MRW and macular parameters. Comparisons of baseline demographics were made between glaucoma and non-glaucoma participants. Receiver operating characteristic (ROC), area under the curve (AUC) and threshold analysis were used to report sensitivity at 0.95 specificity and specificity at 0.95 sensitivity.
Results	There were 128 GwNICOLA participants. The glaucoma group was significantly older (65.6 vs 72.3 years $p<0.001$) and had statistically significantly worse mean deviation (MD) than those without glaucoma (MD -8.77 vs -3.46 $p<0.001$). 80 participants had successful imaging with all tests. Standard mean global cRNFL thickness and inferotemporal cRNFL APS 4.1 mm thickness had the highest sensitivity at 0.95 specificity (0.567). Of these parameters inferotemporal cRNFL APS 4.1 mm thickness had the highest specificity at 0.95 sensitivity (0.300 versus 0.220). mRNFL PPAA mean inferior hemisphere had the highest sensitivity at 0.95 specificity (0.467) among macular parameters.
Conclusion	Standard mean global cRNFL thickness and inferotemporal cRNFL APS 4.1 mm thickness parameters had the highest sensitivity at 0.95 specificity. Macular SD-OCT parameters did not show higher sensitivity at 0.95 specificity than cRNFL parameters in this population.

Date	April 2019
Event/location	NERI Seminar
Title	Why are Disability Rates in Northern Ireland so High
Authors	Anne Devlin

Purpose	Northern Ireland has historically had high levels of working-age economic inactivity compared to the other UK constituent countries, the principal component of which is inactivity on the grounds of illness or disability. Northern Ireland also has considerably higher rates of disability-related benefit claiming compared to most other parts of the UK, e.g. Employment Support Allowance / Incapacity Benefit claimant rates in Northern Ireland are double those in England. This research aims to find the drivers behind these higher rates of disability. Exploiting newly available data from the NICOLA and ELSA surveys we show that the drivers behind the high rates of disability in NI are not in line with the current literature in the area. We find interesting results, particularly for disability benefit receipt. Our findings have several policy implications for both NI and the UK.

Date	September 2019
Event/location	16th NuGO conference, Bern
Title	Novel dietary biomarker candidates identified through a combined NMR and LCMS metabolomics approach
Authors	G. Rosas da Silva, S.F. Graham, Z. Ugur, A. Yilmaz, F. Kee, I. Young, J.V. Woodside and B.D. Green
Purpose	Nutritional biomarkers are biological indicators of nutritional status reflecting the consumption or metabolism of dietary constituents. It is now possible to investigate biochemical markers systematically using metabolomics tools to improve dietary assessment techniques such as food frequency questionnaires and food diaries. The aim of the current project was to discover new dietary biomarkers by performing both NMR and LC-MS-based metabolomics analyses on serum samples collected within NICOLA (Northern Ireland Cohort for the Longitudinal Study of Ageing).
Methods	Samples and data were provided from a dietary validation subset of NICOLA participants, comprised of 95 individuals. Blood samples from individuals were collected at baseline and with a 6 month follow-up, each with coinciding nutritional information (four-day food diary). Samples were prepared and analysed by two complementary metabolomic platforms. UPLC-MS analysis involved a Waters TQ-S coupled with an Acquity I-class UPLC, used in combination with a targeted metabolomics kit (AbsoluteIDQ p180 kit, Biocrates Life Sciences), with acquired data processed using MassLynx v4.1 and MetIDQ software. NMR analysis involved the use of a Bruker 600MHz Ascent coupled to a TCI cryoprobe, with acquired spectra analysed using Bayesil software (University of Alberta, Canada). Statistical analysis of quantified metabolites and food consumption was performed using SPSS.
Results	A total of 15 statistically significant ($p<0.05$) food-metabolite correlations were detected after adjusting for age, sex and BMI. Strong correlations between dairy consumption and specific serum glycerophospholipids were detected, and also between fruit and serum levels of acetic acid. Gender-specific associations of dairy consumption and glycerophospholipids were particularly strong. Some of these findings were supportive of previously published dietary biomarkers.

Conclusion	This study brings forward new information to assist with the discovery of reliable and reproducible nutritional biomarkers. Further validation studies are required in other cohorts/populations to improve confidence in the discovered biomarkers.

Date	October 2019
Event/location	FENS
Title	Combined LC-MS and ^{1}H-NMR metabolomic profiling uncovers dietary biomarkers in a cohort of healthy Northern Irish older adults
Authors	Goncalo Rosas da Silva, Stewart F Graham, Ali Yilmaz, Zafer Ugur, Ian Young, Frank Kee, Charlotte E Neville, Jayne Woodside, Brian D Green
Purpose	A long standing issue in the field of nutrition is the potential inaccuracy of methods traditionally used for dietary assessment (i.e. food diaries and food frequency questionnaires). It is possible to overcome the limitations and biases of these techniques by combining them with analytical measurements in human biofluids. Metabolomic technologies are gaining popularity as nutritional tools due to their capacity to measure metabolic responses to external stimuli, such as the ingestion of certain foods. This project performed both LC-MS and ^{1}H-NMR metabolomic profiling on serum samples collected as part of the NICOLA study (Northern Irish Cohort for the Longitudinal Study of Aging) in order to discover novel dietary biomarkers.
Methods	A dietary validation cohort (NIDAS) was incorporated within NICOLA, involving 95 individuals (45 males, 50 females, aged 50 years and over). Participants provided detailed dietary data (4-day food diary) and blood samples at two time-points, six months apart. Serum samples were processed on two analytical platforms. ^{1}H-NMR spectra were acquired using a Bruker 600MHz Ascent coupled to a TCI cryoprobe and processed using Bayesil (University of Alberta, Canada). A Waters TQ-S coupled with an Acquity I-class UPLC was used in combination with a targeted commercially available kit (AbsoluteIDQ p180 kit, Biocrates). Mass spectra obtained were processed with MetIDQ and verified using MassLynx (v4.1). Data were tested for normality, and serum metabolite concentrations were correlated with recorded dietary intake of each food type using SPSS.
Results	More than 50 statistically significant ($P<0.05$) food-metabolite correlations were detected, 15 of which remained significant after eliminating potential confounding from sex, age and BMI. The strongest correlations were between fruit consumption and acetic acid, and between dairy consumption and certain glycerophospholipids (e.g. LysoPC aa C20:3). Stratifying the cohort by gender yielded further correlations, these included PC ae C38:2 (dairy; males), PC aa C34:4 (dairy; females), PC aa C36:4 (dairy; females), Glutamine (fruit; males) and trans-4-Hydroxyproline (meat; males).

Conclusion	A number of potential blood-based food biomarkers were detected, many of which are gender-specific, and some are corroborated by previously published studies. However, further validation work is required. For example, biological plausibility needs to be established, and the findings need to be reproduced in other cohorts to demonstrate their applicability in larger and more diverse populations. These results contribute greatly to the ongoing efforts to discover and validate reliable nutritional biomarkers as an objective and unbiased measurement of food intake.

Date	October 2019
Event/location	FENS
Title	Relative validity of fruit and vegetable intakes estimated from a food frequency questionnaire (FFQ): the Northern Ireland Cohort for the Longitudinal Study of Ageing (NICOLA).
Authors	Charlotte E Neville, Michelle C McKinley, Frank Kee, Ian S Young, Chris R Cardwell, Jayne V Woodside
Purpose	Accurate assessment of dietary intake in older populations is important for determining the role of diet in healthy ageing. The food frequency questionnaire (FFQ) is a commonly used dietary assessment tool, however there is limited evidence regarding its utility for accurately assessing fruit and vegetable (FV) intake in older adults. The objective of this study was to validate FV intakes estimated from the FFQ used in the Northern Ireland Cohort for the Longitudinal Study of Ageing (NICOLA) against a food diary (FD).
Methods	A dietary validation study was conducted in a sub-sample of 95 participants (45 males, 50 females, aged >50 years) from NICOLA. Participants were asked to complete a FFQ and 4-day FD (reference method) at two time-points (Month 0 and Month 6). Self-reported FV intakes were compared between methods using Spearman's correlation coefficients, examining the percentage of participants classified into the same or adjacent quartile of FV intake, weighted kappa and Bland-Altman plots.
Results	Median fruit, vegetable and total FV intake were significantly higher in the FFQ than the FD at both Month 0 and Month 6 (all $p<0.001$). Significant positive correlations (all $p<0.05$) were observed between the FFQ and FD estimates of FV intake at both time-points (Month 0, $r=0.57$, 0.50 and 0.49 for fruit, vegetables, total FV, respectively; Month 6 $r=0.56$, 0.42 and 0.50, respectively). When FV intakes were classified into fourths (based upon quartiles of total FV portions by FD or FFQ), 80% and 79% of participants were classified into the same or adjacent quartile at Month 0 and Month 6, respectively. Weighted kappa indicated a fair-moderate agreement between the two methods for FV intake (weighted kappa=0.35 and 0.37 at Month 0 and Month 6, respectively). Bland-Altman plots showed that, as FV intake increased, there was a widening in limits of agreements, between the FFQ and FD. There was also a significant positive correlation noted between total FV intakes reported at Month 0 and those reported at Month 6 ($r=0.70$, $p<0.001$).

Conclusion	Over-reporting of FV intake was evident with the FFQ compared to the FD, however, the results showed good comparability between the methods in being able to rank older adults according to their FV intake. An additional analysis of FV biomarkers obtained from this sample will provide a more objective assessment of FV intake by each method.

Date	2nd – 3rd May 2019
Event/location	TILDA Scientific Conference, Westport, Co.Mayo, Ireland
Title	Dietary intake measurements of older adults in NI: NICOLA
Authors	Charlotte Neville, Michelle C McKinley, Frank Kee, Ian S Young, Chris R Cardwell, Jayne V Woodside
Purpose	Accurate assessment of dietary intake in older populations is important for determining the role of diet in healthy ageing. The food frequency questionnaire (FFQ) is a commonly used dietary assessment tool, however there is limited evidence regarding its utility for accurately assessing dietary intake in older adults. It is therefore important that such dietary assessment methods are validated in older populations and that other methods for assessing dietary intake, such as biomarkers, are explored.
Methods	The Northern Ireland Cohort for the Longitudinal Study of Ageing (NICOLA) has collected a wealth of nutritional data from over 2,500 older adults including anthropometric measurements, self-reported dietary intakes via a FFQ and biological markers. A dietary validation study was also conducted in a sub-sample of 95 NICOLA participants whereby, in addition to completing the 130-item FFQ (EPIC-Norfolk) and giving a blood sample, participants completed a 4-day food diary at two time points (Month 0 and Month 6). Self-reported FV intakes were compared between methods using Spearman's correlation coefficients, examining the percentage of participants classified into the same or adjacent quartile of FV intake, weighted kappa and Bland-Altman plots.
Results	The validation study showed that median fruit, vegetable and total FV intake were significantly higher in the FFQ than the FD at both time-points (all $p<0.001$). Positive correlations (all $p<0.05$) were observed between the FFQ and FD estimates of FV intake (Month 0, $r=0.57$, 0.50 and 0.49 for fruit, vegetables, total FV, respectively; Month 6, $r=0.56$, 0.42 and 0.50, respectively). When FV intakes were classified into fourths (based upon quartiles of total FV portions by FD or FFQ), 80% and 79% of participants were classified into the same or adjacent quartile at Month 0 and 6, respectively. Weighted kappa indicated a fair-moderate agreement between the two methods for FV intake ($\kappa = 0.35$ and 0.37 at Month 0 and 6, respectively). Bland-Altman plots showed that, as FV intake increased, there was a widening in limits of agreements, between the FFQ and FD. Positive correlations were also noted between FV intakes reported at Month 0 and those reported at Month 6 ($r=0.70$, $p<0.001$).

Conclusion	Over-reporting of FV intake was evident with the FFQ compared to the FD, however, the results showed good comparability between methods in being able to rank older adults according to their FV intake. Further in-depth dietary analyses are being conducted within NICOLA including nutrient analysis, dietary pattern analysis, biomarker analysis and metabolomic analysis of biological samples. Using multiple dietary assessments methods and/or biomarker approaches may provide a more accurate estimate of true dietary intake and enable more accurate diet-disease relationships in older adults to be established. This research will correct the lack of dietary validation studies in older adults to date. It will also unravel the potential role of diet in healthy ageing and will ultimately lead to appropriate, evidence-based, dietary guidelines for older people to promote healthy ageing, in the context of an ageing population worldwide.

Date	25 – 30 August 2019
Event/location	19th International Symposium on Toxicity Assessment - ISTA19, Greece
Title	Arsenic exposure in relation to diet and geography in adults higher than 50 years from Northern Ireland
Authors	NV de Moraes, M Carey, CE Neville, F Kee, IS Young, JV Woodside, A Meharg
Purpose	Arsenic (As) exposure has been associated with increased cancer risk, even when exposure occurs at low levels. Previous work has shown potential associations of high arsenic concentration in soils with stomach cancer in some regions of Northern Ireland (NI).
Methods	This study was conducted in a sub-sample of 89 participants of the NI Cohort for the Longitudinal Study of Aging (NICOLA) study, which recruited a random sample of people aged >50 years living in their own homes in NI. Spot urine samples were collected from 87 participants for determination of As species. Each participant recorded all drinks and food consumed over four consecutive days in food diaries. The inorganic arsenic (iAs), monomethylarsonic acid (MMA), dimethylarsinic acid (DMA) and arsenobetaine (AsB) were analysed in urine (U) using ion chromatography with inductive coupled plasma mass spectrometry (IC-ICP-MS).
Results	Exposure to arsenic was low but highly variable, with median (5-95th percentiles) urinary concentrations of 0.33 (0.09-1.00 µg/L), 0.32 (0.10-0.92 µg/L), 1.92 (0.58-7.53 µg/L) and 2.28 (0.13-62.46 µg/L) for iAs, MMA, DMA and AsB, respectively. Multiple linear regression analysis was performed to identify the main predictors of As exposure. Both dairy products and tap water intake showed a negative association with urinary concentrations of iAs, MMA and DMA. Dairy consumption was the best predictor of iAs and DMA in urine, explaining 15.9 and 14.6% of the variability, respectively. Tap water was the best predictor for MMA and explained 15.4% of the variability. Alcohol consumption showed a positive association with iAs in urine and explained 8.9% of its variability. Seafood intake showed a significant positive association with AsB and DMA in urine, and explained 16 and 7.5% of their variability, respectively. Rice consumption was not associated with arsenic exposure in this cohort. The residence area in NI was associated with log-transformed urinary concentrations of MMA and iAs+MMA+DMA (One-way ANOVA, $p<0.05$). However, multiple regression analysis showed that geography is not a

	relevant predictor of As exposure in NI. Principal component analysis (PCA) was in agreement with the previous results which showed that seafood had a positive association with DMA and AsB, while tap water and dairy products showed negative associations with As species. All arsenic species clustered together on PCA analysis, and this can be explained by both AsB and the inorganic species (iAs and DMA) having a common source of exposure.
Conclusion	In conclusion, rice was not an important predictor of As exposure in NI. The consumption of water and dairy products may have a diluting effect on As body burden, while seafood intake was the main predictor of AsB and DMA. However, the majority of the variation in As biomarkers in urine was not explained by these analyses.

Date	28th April – 2nd May 2019
Event/location	The Association for Research in Vision and Ophthalmology – Vancouver
Title	Clinical characteristics of diabetes and diabetic retinopathy in an ageing population-NICOLA Study
Authors	Halliday, Sophia; Quinn, Nicola B.; Peto, Tunde; Cruise, Sharon; Wright, David; McGuinness B, Young, I.S.; Kee, Frank, Chakravarthy, Usha; Hogg Ruth.
Purpose	To examine the prevalence diabetic retinopathy (DR) and maculopathy among people with diabetes from the Northern Ireland Cohort of the Longitudinal Study of Aging (NICOLA Study) participants.
Methods	The Northern Ireland Cohort of the Longitudinal Study of Aging (NICOLA Study) is a multidisciplinary longitudinal population-based study of ageing. Retinal imaging at the NICOLA study health assessment included stereo colour fundus photography (Canon CX-1, Tokyo, Japan), spectral domain optical coherence tomography (SD-OCT) ((HRA+OCT; Heidelberg Engineering, Heidelberg, Germany). These were graded by NetwORC UK Ophthalmic Reading Centre. Medical history including medication was obtained during a home interview. A blood sample was used to assess HbA1C and non-fasting glucose level. WHO criteria were used for interpretation of HBA1C to diagnose Diabetes Mellitus (DM) (6-6.4=impaired glucose tolerance,>6.5=DM). Descriptive statistics were used to describe the prevalence of DR.
Results	Of the 3616 participants that completed a health assessment, 196 were home health assessments, a further 27 participants refused retinal imaging. Imaging from 3393 participants were available for analysis. Mean age of the sample was 63.44 (sd. 9.013 range. 36-99). The prevalence of diabetes was analysed through multiple measures including HbA1C, self-report, medication use and blood glucose level. According to the WHO classification 327 participants had diabetes (11.8%) and 310 had impaired glucose regulation (11.1%). Of the 327 participants only 167 (51.1) reported that they had the condition in response to questions in both the home interview and at the health assessment. DR prevalence for those with DM was 11.3% (n=37). The prevalence of maculopathy was 8.3% (n=12). The number of individuals that fall into the categories background retinopathy, pre-proliferative, stable proliferative and active proliferative were 26, 4, 5 and 2 respectively.

Conclusion	This is the largest epidemiological study to date examining the burden of DM or DR in Northern Ireland and one of a few worldwide that has included OCT grading of maculopathy. Findings from this study will have implications for professionals working in the diabetes and sight loss sectors. The relatively large number of participants with high HbA1c who did not appear to be aware they had the condition is of particular concern.

Date	28th April – 2nd May 2019
Event/location	The Association for Research in Vision and Ophthalmology – Vancouver
Title	Prevalence of Age-Related Macular Degeneration Using Multi-Modal Retinal Imaging in a Population Based Aging Cohort: The NICOLA Study
Authors	Ruth Esther Hogg; Nicola Quinn; Tunde Peto; David Wright; Bernadette McGuinness; Ian Young; Frank Kee; Usha Chakravarthy
Purpose	To examine the prevalence age-related macular degeneration (AMD) in Northern Ireland Cohort of the Longitudinal Study of Aging (NICOLA Study) participants using colour fundus photography (CFP) and spectral-domain optical coherence tomography (SD-OCT).
Methods	The Northern Ireland Cohort for the Longitudinal Study of Aging (NICOLA Study) is a multidisciplinary longitudinal population-based study of ageing. Retinal imaging at the NICOLA study health assessment included stereo CFP (Canon CX-1, Tokyo, Japan) and SD-OCT ((HRA+OCT; Heidelberg Engineering, Heidelberg, Germany). Each modality was graded independently for AMD features by NetwORC UK Ophthalmic Reading Centre and incidences of discordance arbitrated by Senior graders, with late AMD verified by Clinicians. Medical history and demographic information was obtained during a home interview. Descriptive statistics were used to describe the prevalence of AMD in terms of the Beckman Clinical Classification and explore the differences in AMD stage and case status by modality.
Results	Retinal images from 3393 participants were available for analysis. Mean age of the sample was 63.44 (sd. 9.013 range. 36-99). Prevalence of AMD using arbitrated colour grading was: No drusen: 59.0 %, drusen <63mm: 16.8 %, drusen 63-125mm:12.1%, drusen>125mm or pigmentary changes: 7.8%, late AMD:0.8%. Prevalence of nodular drusen in eyes on OCT was 34.8% and prevalence of focal atrophy on OCT was 6.1%. There were 1317(19%) eyes in which drusen was initially graded as present on colour but absent on OCT, arbitration using both modalities simultaneously revealed this was commonly caused by: over calling small drusen on CFP (19%), image quality on either modality (31%), subretinal drusenoid deposits on OCT (5%), other pathology causing drusen-like lesions (10%), vitreous changes (2%), drusen outside field of view of OCT (~8%), single drusen on OCT (5%), drusen missed on OCT 11% and 10% in which drusen-like lesions were clearly visible on colour but OCT looked healthy

Conclusion	This is the largest epidemiological study to date examining the burden of AMD in Northern Ireland and one of a few worldwide that has included OCT grading of AMD. Given the substantial discordance between colour alone versus both together there will be challenges in comparing prevalence data with historical cohorts.
Abstract published	Yes
Abstract reference	Investigative Ophthalmology & Visual Science July 2019, Vol.60, 63. doi: https://doi.org/

Date	28th April – 2nd May 2019
Event/location	The Association for Research in Vision and Ophthalmology – Vancouver
Title	Comparison of colour fundus photography and ultra wide field retinal imaging in the detection of choroidal naevi in an ageing population
Authors	Nicola Quinn
Purpose	To determine the prevalence of choroidal naevi in a population based sample of ageing individuals in Northern Ireland and compare their detection using ultra-wide field retinal imaging (UWFI) and colour fundus photography (CFP).
Methods	UWFI (Optomap 200 TX) and CFP images (Canon CX-1, Tokyo, Japan) were obtained from the Northern Ireland Cohort of the Longitudinal Study of Aging (NICOLA Study) participants. The Optomap images were graded for the presence of choroidal naevi using the Manchester Grid (MG), which is composed of 400 cells, each approximately one disc area in size. The retina was divided into regions using defined x- and y-coordinates on the MG to determine the area of the retina corresponding to the CFP images. CFP images were graded for the presence of naevi using Oculab (V3.7.980) imaging platform. All discordant cases were adjudicated by a senior grader. Descriptive statistics were used to describe the prevalence and concordance between imaging modalities for choroidal naevi.
Results	Retinal imaging was available from 3393 participants (6270 eyes for CFP and 6153 eyes for UWF), aged 36-99 (mean 63 years, SD 9.01). In UWFI naevi were found in 486(7.9%) of eyes. In the area corresponding to the field of view of CFP naevi were found in 237 (3.8%) eyes from 103 participants using CFP whereas naevi were identified in 275 (4.5%) eyes using UWFI, from 243 participants. The Kappa value for this comparison was 0.96 indicating almost perfect agreement. In 2 eyes CFP detected naevi were UWFI didn't, in 229 eyes naevi were detected on both UWFI and CFP and in 16 eyes naevi were detected on UWFI but were not detected on CFP.
Conclusions	Previously reported choroidal naevus prevalence rates (0.2% to 30%) vary widely due to different study populations, examination methods used etc. The prevalence rate found in this study was 3.8% and 4.5% for CFP and UWFI respectively. The detection of choroidal naevi using UWFI was superior to that off standard CFP. The reasons behind this may include; the appearance of naevi found on each imaging modality, the different use of lasers with each modality and artefacts present on the images.

Date	28th April – 2nd May 2019
Event/location	The Association for Research in Vision and Ophthalmology – Vancouver
Title	Prevalence and severity of macular holes in an ageing population from Northern Ireland
Authors	Catherine Jamison; Nicola B Quinn; Usha Chakravarthy; Tunde Peto; Frank Kee; Ian Young; Bernadette McGuinness; Ruth Hogg
Purpose	To determine the prevalence and severity stage of macular holes in patients who participated in the Northern Ireland Cohort for the Longitudinal Study of Ageing (NICOLA)
Methods	The NICOLA study is a multidisciplinary longitudinal population based study of ageing. Retinal imaging at the NICOLA study health assessment included stereo colour fundus photography (Canon CX-1, Tokyo, Japan), spectral domain optical coherence tomography (SD-OCT) (HRA+OCT; Heidelberg Engineering, Heidelberg, Germany). These were graded by NetwORC UK ophthalmic Reading Centre. Macular holes were reported under 'Other Pathology'. Images for eyes selected as having macular hole then regraded and staging added for those that were deemed a 'true' macular hole, if participants had attended follow-up studies and images were available; these were also examined and staged.
Results	Of the 3393 patients (mean age 63, S.D. 9.03) who attended the eye component of the study there were 6611 eyes (97%) with gradable OCT cube scans. The prevalence of any stage of a macular hole was 0.008%, with 54 eyes from 53 patients graded as having some stage of macular hole. A total of six out of 56 eyes (10.7 %) were diagnosed with a true macular hole, 19 (33.9%) with a pseudo-hole due to epiretinal membrane (ERM), 13 (23.2%) with abnormal foveal contour (AFC), nine (16.1%) with a lamellar hole, four (7.1%) with cysts, and three (5.4%) with vitreomacular traction (VMT)-related changes. The six true macular holes consisted of 4 (66.7%) stage 4 macular holes and 2 (33.3%) stage 1 macular holes. Six eyes had follow up visits and of these; one stage 4 macular hole remained the same 22 months later, two AFCs did not change between visits (20, and 22 months later), one VMT resolved at follow-up 21 months later, one did not have OCT images for the return visit, and a case of pseudohole due to ERM, that had progressed to a stage 4 macular hole 17 months later.
Conclusion	Macular holes can be difficult to study due to low prevalence in the general population. The use of OCT enabled differentiation between degrees of macular hole, showing that the majority of cases were pseudo-holes due to ERM and VMT, or lamellar holes, with true macular holes accounting for 10.7 % of eyes. Where true macular holes did occur, these were predominantly advanced.
Abstract published	Yes
Abstract reference	Investigative Ophthalmology & Visual Science July 2019, Vol.60, 3951. doi:https://doi.org/

Date	16th -18th May
Event/location	EASD Eye Complications Study Group – Amsterdam, Netherlands
Title	Clinical characteristics of the peripheral retina in people with diabetes

Authors	Nicola Quinn, Sophia Halliday, Tunde Peto, Usha Charavarthy, Bernadette McGuinness, Sharon Cruise, Frank Kee, Ian Young, Ruth Hogg
Purpose	To record the frequency of retinal haemorrhages in the central and peripheral retina using ultra-wide field retinal images (UWFI) of those participants of Northern Ireland Cohort of the Longitudinal Study of Aging (NICOLA Study) who either self-reported diabetes or have haemoglobin A1c (HbA1c) levels of 6/5% and greater.
Methods	UWFI (Optomap 200 Tx) were obtained from the all participants. Optomap images were graded of the relevant NICOLA-participants for the presence of haemorrhages using the Manchester grid (MG) composed of 400 cells, each approximately one disc area in size. The retina was divided into regions using defined x- and y-coordinates on the MG to determine the central and peripheral retina. Cross-tabs were used to compare the frequency of haemorrhages in the different regions of the retina.
Results	Altogether, 111 patients (222 eyes) with self-reported diabetes were available for analysis. 204 eyes (92%) had no observable abnormality either in the centre or peripheral retina; 18 eyes (8%) had haemorrhages present. Of these, 3 (1%) had haemorrhages both in the central and peripheral region; 15 (7%) with only in the peripheral retina. For those with HbA1c >6.5%, 185 participants (370 eyes) were diagnosed with diabetes. No observable abnormality in either the centre or peripheral retina was found in 349 eyes (94%); while 21 (6%) had haemorrhages: 18 (5%) of them only in the peripheral, while 3 eyes (1%) both the centre and peripheral retina.
Conclusion	Our results agree that it is vital to investigate both the central and peripheral retina as haemorrhages can affect the peripheral retina only. There was relatively little concordance between self-reported diabetes and high HbA1C%, hence reporting them as two separate cohorts, highlighting the importance of clear diagnostic guidelines in population based studies.

Date	6 – 7th June 2019
Event/location	European Eye Epidemiology E3 Congress, QUB, Belfast
Title	Glaucoma in the Northern Ireland Cohort for the Longitudinal Study of Aging: Prevalence of glaucoma and factors associated with glaucoma and glaucoma related parameters
Authors	Paul McCann / Ruth Hogg

Date	6 – 7th June 2019
Event/location	European Eye Epidemiology E3 Congress, QUB, Belfast
Title	The NICOLA Study
Authors	Frank Kee

Date	18th June 2019
Event/location	CHARMS event: Health costs of war and trauma workshop, Riddell Hall, QUB, Belfast,
Title	Work disability and the Northern Irish Troubles
Authors	Declan French

Date	18th June 2019
Event/location	CHARMS event: Health costs of war and trauma workshop, Riddell Hall, QUB, Belfast
Title	The mental health consequences and costs of the N. Ireland conflict
Authors	Michael Duffy / Ciaran Mulholland

Date	June 2019
Event/location	European Eye Epidemiology (E3) Congress, QUB, Belfast
Title	Glaucoma in the Northern Ireland Cohort for the Longitudinal Study of Aging: Prevalence of glaucoma and factors associated with glaucoma and glaucoma related parameters
Authors	Paul McCann / Ruth Hogg

2020

Date	3rd-4th Feb 2020
Event/location	British and Irish Longitudinal Studies of Ageing Meeting
Title	Alcohol patterns and cognitive performance among older adults living in the North and South of Ireland
Authors	Claire McEvoy, Viveka Guzman, Joanna McHugh-Power, Joanne Feeney

Date	3rd-4th Feb 2020
Event/location	British and Irish Longitudinal Studies of Ageing Meeting
Title	Loneliness and social isolation among older people in N.Ireland - results from Wave 1 of NICOLA
Authors	Paula Devine

Date	3rd-4th Feb 2020
Event/location	British and Irish Longitudinal Studies of Ageing Meeting
Title	Assessing the relationship between anticholinergic medication and cognition: a retrospective analysis using data from the Northern Ireland Cohort of Longitudinal Ageing
Authors	Alan McMichael, Bernadette McGuinness

Date	3rd-4th Feb 2020
Event/location	British and Irish Longitudinal Studies of Ageing Meeting
Title	Tests for associations of retinal microvascular parameters with impaired renal function in NICOLA
Authors	Ruth Hogg

Date	3rd-4th Feb 2020
Event/location	British and Irish Longitudinal Studies of Ageing Meeting
Title	Data Linkage in the Northern Ireland Cohort for the Longitudinal Study of Ageing
Authors	Frances Burns

Date	May 2020
Event/location	Psychology, Health and Medicine Conference, UCC
Title	Self-reported age related hearing loss and its impact on cognitive and social functioning: A mixed methodology study
Authors	Joanna McHugh Power, Elizabeth Fowler, Joanne Feeney, Annalisa Setti, David Loughrey, Jayne Woodside, Frank Kee, Sharon Cruise, Brian Lawlor

Date	May 2020
Event/location	Psychology, Health and Medicine Conference, UCC
Title	Experiences in the Troubles Moderate the Association Between Social Activity Engagement and Cognitive Functioning: Results from NICOLA
Authors	Joanna McHugh Power, Joanne Feeney, Elizabeth Fowler, Sharon Cruise, Ian Young, Bernadette McGuinness, Frank Kee

Date	27-29 May 2020 (online)
Event/location	European Society for Clinical Investigation
Title	Assessing the utility of metabolite profiles of human serum and urine for determining dietary intake
Authors	Goncalo Rosas da Silva, Brian Green

Date	26-30th July 2020 (online)
Event/location	Alzheimers Association International Conference, Amsterdam
Title	Variation in retinal microvascular parameters were not associated with mild cognitive impairment
Authors	Gareth McKay

Date	May 2020
Event/location	Psychology, Health and Medicine Conference, UCC
Title	Loneliness and healthcare use in Ireland and Northern Ireland: associations in two different healthcare systems
Authors	Dr Annette Burns, Prof Gerry Leavey, Dr Mark Ward, Prof Roger O'Sullivan

Date	21 April 2020
Event/location	NIA biomarker network meeting on functional genomics (RNA and epigenetics) in population health studies

Title	NICOLAs bioresource: understanding today for a healthier tomorrow
Authors	Amy Jayne McKnight

Date	05 Nov 2020
Event/location	GSA 2020 Annual Scientific Meeting
Title	Does loneliness lead to increased healthcare use in older adults?
Authors	Roger O'Sullivan, G Leavey, Annette Burns

Date	05 Nov 2020
Event/location	GSA 2020 Annual Scientific Meeting
Title	Loneliness and social isolation among older people in N.Ireland – results from Wave 1 NICOLA
Authors	Paula Devine, Charlotte Neville

Date	09 Oct 2020
Event/location	Society for Longitudinal Studies International Showcase Workshop
Title	NICOLA Study – Understanding today for a healthier tomorrow
Authors	Charlotte Neville

Date	Oct 2020
Event/location	30th Alzheimers Europe Conference
Title	Assessing the effect of prescription rate of anticholinergic medications on cognitive decline
Authors	Evi Zafeiridi